Serial No.: 10/055,817
Group Art Unit No.: 1615

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended): A pharmaceutical composition comprising the hydrochloride salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide in combination with one or more pharmaceutically acceptable carriers, wherein at least some of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is in granulated form,

~~and~~ wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is present in the composition in at least 4 weight % by weight of the composition~~.~~,

wherein the granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have been formed in the presence of a granulating solvent (i.e. using a "wet granulation" process),

wherein the granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a filler (diluent),

and wherein the filler comprises a pharmaceutically acceptable calcium or magnesium salt which is a phosphate, hydrogen phosphate, carbonate or hydrogen carbonate salt and which is insoluble, practically insoluble, very slightly soluble or slightly soluble in the granulating solvent.

2. (Previously Presented): A composition as claimed in claim 1 wherein substantially all of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is in granulated form.

3. (Previously Presented): A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of $\geq$ 100 microns.

4. (Previously Presented): A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≥ 250 microns.

5. (Previously Presented): A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of 100 to 1000 microns.

6. (Previously Presented): A composition as claimed in claim 1 wherein 90% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≥ 10 microns.

7. (Previously Presented): A composition as claimed in claim 1 wherein 90% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≥ 50 microns.

8. (Previously Presented): A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the particles of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≤ 50 microns.

9. (Previously Presented): A composition as claimed in claim 1 wherein 10% or more by weight or by volume of the particles of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≤ 10 microns.

10. (Previously Presented): A composition as claimed in claim 1 wherein 50% or more by weight or by volume of the granules including the N-[(1-^{n}butyl-4-

piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≥ 100 microns (micrometres); and wherein 10% or more by weight or by volume of the particles of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt have a particle size of ≤ 10 microns.

11. (Previously Presented): A composition as claimed in claim 1 wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is present in the composition in at least 5 weight % by weight of the composition.

12. (Previously Presented): A composition as claimed in claim 1 wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is present in the composition in at least 6 weight % by weight of the composition.

13. (Previously Presented): A composition as claimed in claim 1 wherein the hydrochloride salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide is of a form obtainable by a process in which the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is dissolved in ethanol or an ethanol-containing solvent to form a solution and is crystallised from the solution by addition of a C_5-C_{10} hydrocarbon and/or a solvent containing a C_5-C_{10} hydrocarbon.

14. (Currently Amended): A composition as claimed in claim 1 wherein the weight ratio of the filler to drug in the granules is at least 1:2, and wherein the filler is present in ≥ 15 weight % of the composition. ~~granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a filler/diluent.~~

15. (Currently Amended): A composition as claimed in claim 1 ~~14~~ wherein the filler/diluent is abrasive.

16. (Currently Amended): A composition as claimed in claim 1 ~~14~~ wherein the filler/diluent is insoluble, practically insoluble, very slightly soluble or slightly soluble in water and/or ethanol.

17. (Currently Amended): A composition as claimed in claim 1 ~~14~~ wherein the filler/diluent is insoluble or practically insoluble in water and/or ethanol.

18. (Currently Amended): A composition as claimed in claim 1 ~~14~~ wherein the filler includes calcium phosphate, dibasic calcium phosphate, calcium carbonate, magnesium carbonate and/or magnesium phosphate ~~comprises any pharmaceutically acceptable metal salt which is insoluble, practically insoluble, very slightly soluble or slightly soluble in water and/or ethanol.~~

19. (Currently Amended): A composition as claimed in claim 1 wherein the ~~the granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a~~ filler/diluent in the granules comprises~~ing~~ $CaHPO_4$ (i.e. dibasic calcium phosphate, dicalcium phosphate, calcium hydrogen phosphate) and/or $Ca_3(PO_4)_2$ (i.e. calcium phosphate, tribasic calcium phosphate).

20. (Currently Amended): A composition as claimed in claim 1 or 19, wherein the weight ratio of the filler to drug in the granules is at least 1:3, and wherein the filler is present in ≥ 15 weight % of the composition.

21. (Currently Amended): A composition as claimed in claim 1 ~~16~~, wherein the filler is present in from 15 to 85% by weight of the composition.

22. (Currently Amended): A composition as claimed in claim 1 ~~16~~ including a binder present in about 1 to about 10 weight % of the composition, and wherein the binder is soluble, freely soluble or very soluble in water.

23. (Currently Amended): A composition as claimed in claim 22 wherein the binder comprises hydroxypropylmethylcellulose, hydroxypropylcellulose , hydroxyethylcellulose,

hydroxymethylcellulose, methyl cellulose, ethyl cellulose, or povidone (polyvinylpyrollidone).

24. (Previously presented): A composition as claimed in claim 1, 3 or 19 including an excipient which acts as a compression and/or granulation aid.

25. (Previously Presented): A composition as claimed in claim 1 being a tablet, or a capsule containing said composition.

26. (Currently Amended): A method of making a pharmaceutical composition comprising the hydrochloride salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide in combination with one or more pharmaceutically acceptable carriers, wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is present in the composition in at least 4 weight % by weight of the composition,

the method comprising forming at least some of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt into granules~~.~~ in the presence of a granulating solvent (i.e. using a "wet granulation" process),

the method also comprising mixing some or all of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt with a filler (diluent) before granulation so that the granules also contain the filler (diluent),

and wherein the filler comprises a pharmaceutically acceptable calcium or magnesium salt which is a phosphate, hydrogen phosphate, carbonate or hydrogen carbonate salt and which is insoluble, practically insoluble, very slightly soluble or slightly soluble in the granulating solvent.

27. (Currently Amended): A method as claimed in claim 26 comprising mixing some or all of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt with microcrystalline cellulose ~~a filler (diluent), and optionally a compression and/or granulation aid,~~ before granulation.

28. (Currently Amended): A method as claimed in claim 26 ~~27~~ wherein the ~~granules are formed in the presence of a~~ granulating solvent comprises water and/or ethanol and/or is isopropanol ~~using a wet granulation process~~.

29. (Currently Amended): A method as claimed in claim 28 wherein the granulating solvent is water ~~the filler is insoluble, practically insoluble, very slightly soluble or slightly soluble in the granulation solvent~~.

30. (Currently Amended): A method as claimed in claim 26 ~~29~~ wherein after formation the granules are milled to a particle size suitable for use in tablets or capsules.

31. (Previously presented): A method as claimed in claim 26 wherein, after being formed and optionally milled, the granules are mixed with other pharmaceutically acceptable excipient(s) and compressed into tablets or filled into capsules.

32. (Currently Amended): A method of making a pharmaceutical composition comprising the hydrochloride salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide in combination with one or more pharmaceutically acceptable carriers, wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt is present in the composition in at least 4 weight % by weight of the composition

the method comprising:

(a) dissolving the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt in ethanol or an ethanol-containing solvent to form a solution,

(b) crystallising the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt from the solution by addition of a C_5-C_{10} hydrocarbon and/or a solvent containing a C_5-C_{10} hydrocarbon, and

(c) forming at least some of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt into granules~~.~~ in the presence of a granulating solvent (i.e. using a "wet granulation" process);

wherein step (c) also comprises mixing some or all of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide

hydrochloride salt with a filler (diluent) before granulation so that the granules also contain the filler (diluent),

and wherein the filler comprises a pharmaceutically acceptable calcium or magnesium salt which is a phosphate, hydrogen phosphate, carbonate or hydrogen carbonate salt and which is insoluble, practically insoluble, very slightly soluble or slightly soluble in the granulating solvent.

33. (Previously Presented): A method as claimed in claim 32 wherein 50% or more by weight or by volume of the granules including the hydrochloride salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide have a particle size of ≥ 100 microns.

34. (Previously Presented): A method as claimed in claim 33 comprising the additional step after formation of the granules of (d) mixing the granules with other pharmaceutically acceptable excipient(s) and compressing into tablets or filling into capsules.

35. (Previously Presented): A composition as claimed in claim 1, wherein the HCl salt of N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide is of a form obtainable by a process in which the HCl salt is dissolved in ethanol or an ethanol-containing solvent to form a solution and is crystallised from the solution by addition of a C_5-C_{10} hydrocarbon and/or a solvent containing a C_5-C_{10} hydrocarbon.

36. (Previously Presented): A composition as claimed in claim 1, wherein the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide or salt thereof is present in the composition in up to 70 weight % by weight of the composition.

37. (Previously Presented): A composition as claimed in claim 3, wherein the granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a filler comprising $CaHPO_4$ and/or $Ca_3(PO_4)_2$, wherein the weight ratio of the filler to drug in the granules is at least 1:3, and wherein the filler is present in ≥ 15 weight % of the composition.

38. (Currently Amended): A composition as claimed in claim 1 wherein the ~~granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a~~ filler in the granules comprises~~ing~~ dibasic calcium phosphate dehydrate (i.e. $CaHPO_4.2H_2O$).

39. (Currently Amended): A composition as claimed in claim 1 wherein the filler (diluent) in the granules comprises ~~containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a fine grade filler (diluent) being~~ fine grade $CaHPO_4$ or fine grade $Ca_3(PO_4)_2$.

40. (Currently Amended): A composition as claimed in claim 24, wherein the compression and/or granulation aid is present inside the granules of the composition~~.~~, which does not exclude the possibility that a portion is optionally present outside the granules.

41. (Previously Presented): A composition as claimed in claim 40, wherein the compression and/or granulation aid is present in at least 15 weight % of the composition.

42. (Previously Presented): A composition as claimed in claim 41, wherein the compression and/or granulation aid is microcrystalline cellulose.

43. (Previously Presented): A composition as claimed in claim 24, wherein the compression and/or granulation aid is microcrystalline cellulose.

44. (Previously Presented): A composition as claimed in claim 1 or 19, wherein the composition includes a disintegrant present in about 1 to about 10 weight % of the composition and a lubricant present in about 0.2 to about 5 weight % of the composition.

45. (Currently Amended): A composition as claimed in claim 42, wherein the ~~granules containing the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt also contain a~~ filler in the granules comprises~~ing~~ $CaHPO_4$ and/or $Ca_3(PO_4)_2$, wherein the weight ratio of the filler to drug in the granules is at least 1:3, and wherein the filler is present in $\geq$ 15 weight % of the composition.

46. (Previously Presented): A composition as claimed in claim 45, wherein the composition includes a disintegrant present in about 1 to about 10 weight % of the composition and a lubricant present in about 0.2 to about 5 weight % of the composition.

47. (Previously Presented): A composition as claimed in claim 1, 3 or 19, wherein the intragranular ingredients form ≥ 70% by weight of the composition.

48. (Previously Presented): A composition as claimed in claim 45, wherein the intragranular ingredients form ≥ 70% by weight of the composition.

49. (Currently Amended): A composition as claimed in claim 1, 3, 16 or 19, wherein the ~~granules have been formed in the presence of a~~ granulating solvent comprises water and/or ethanol and/or isopropanol ~~using a wet granulation process~~.

50. (Currently Amended): A composition as claimed in claim 45, wherein the ~~granules have been formed in the presence of a~~ granulating solvent comprises water ~~using a wet granulation process~~.

51. (Currently Amended): A method as claimed in claim 26 or 32 comprising:

mixing some or all of the N-[(1-^{n}butyl-4-piperidinyl)methyl]-3,4-dihydro-2H-[1,3]oxazino[3,2-a]indole-10-carboxamide hydrochloride salt with a filler (diluent) comprising $CaHPO_4$ and/or $Ca_3(PO_4)_2$, and with microcrystalline cellulose, before granulation,

wherein the weight ratio of the filler to drug in the granules is at least 1:3, and wherein the filler is present in ≥ 15 weight % of the composition,

and wherein the microcrystalline cellulose is present in at least 15 weight % of the composition, and the microcrystalline cellulose is present inside the granules of the composition ~~is intragranular but~~ which does not exclude the possibility that a portion is optionally present outside the granules.

and wherein the granules are formed in the presence of a granulating solvent using a wet granulation process.